(ii) transforming the cell of (i) or a descendent of the cell by integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells from the cell of (ii); and

(iv) selecting tissue or specialized cells of (iii) by the presence of a detectable indicator resulting from both the first and second indicator components.

REMARKS

With entry of this amendment, claims 1-6, 9 and 12-19 are pending in the application. Claims 9, 12 and 15 have been incated to be allowable by the Examiner. Claims 1-6, 13, 14 and 16-18 were rejected under 35 U.S.C. 112, first paragraph, as allegedly nonenabled. For the reasons set forth herein, this rejection is overcome.

The Claims

In order to expedite prosecution, claims 2 and 14 have been canceled without prejudice.

Claims 1, 6, 13 and 18 have been amended. Support for the amendments to the claims is found, *inter alia*, throughout the specification. More particularly, support for the amendment to claim 1 is found, *inter alia*, on page 28, lines 19-36, of the specification. Support for the amendment to claim 6 is found in claim 1 as originally filed. Support for the amendment to claim 13 is found on page 28, lines 19-36, of the specification, and in claim 1 as originally filed. Support for the amendment to claim 18 is found on page 28, lines 19-36, of the specification. No new matter has been added. In view of the foregoing support, Applicants respectfully request that the Examiner enter the amendments.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 13, 14 and 16-18 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly being nonenabled. The Examiner acknowledges that the specification is enabling for methods of screening for integration of a DNA construct into a target gene having expression restricted to a specific eukaryotic tissue or specialized eukaryotic cell *in vitro* or in a mouse, wherein two DNA constructs encoding separate indicator components are integrated into a cell, which is not a non-mouse ES cell, and which is subsequently used to form a tissue or specialized cell *in vitro* or to form a mouse. However, the Office Action alleges that the specification is not enabling for use of ES cells from an organism other than a mouse. To the extent that the rejection is applicable to the amended set of claims, Applicants respectfully traverse.

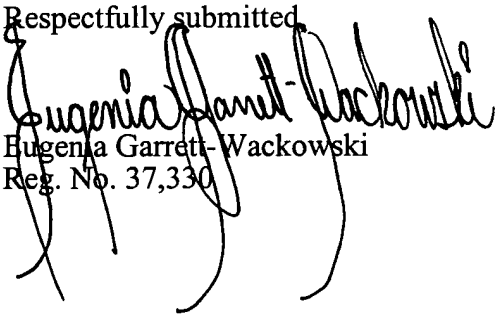
In order to expedite prosecution, Applicants have amended claims 1, 6, 13 and 18 to specify murine ES cells and mice, thus rendering the rejection moot. As the Examiner has pointed out, the specification is enabling for methods of screening for integration of a DNA construct into a target gene having expression restricted to a specific tissue or cell in a mouse. Since the claims now relate to methods in mouse cells and mice, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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PATENT

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claims 2 and 14 have been canceled.

Claims 1, 6, 13, and 18 have been amended as follows:

1. (Amended) A method of screening for the integration of a DNA construct into a target gene having restricted expression in a [eukaryotic organism] mouse, said method comprising:

(i) transforming a [eukaryotic] murine ES cell with a first DNA construct encoding a first indicator component under the control of a promoter having restricted expression in a mouse;

(ii) transforming the cell of (i) or a descendent of the cell by operably integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells from the cell of (ii); and

(iv) monitoring the tissue or specialized cells of (iii) for a detectable indicator resulting from both the first and second indicator components indicative of integration of the second DNA construct into a gene having restricted expression

6. (Amended) The method of claim 1 which additionally comprises isolating DNA endogenous to the [eucaryotic] cell or descendent thereof which flanks the second DNA construct integrated into a gene having restricted expression.

13. (Amended) A [eukaryotic] murine ES cell or descendent thereof, transformed by the combination of DNA constructs of claim 12.

18. (Amended) A method of producing [eukaryotic] murine tissue or specialized cells comprising a detectable indicator associated with a target gene having restricted expression, which comprises:

(i) transforming a [eukaryotic] murine ES cell with a first DNA construct encoding a first indicator component under the control of a promoter having restricted expression in a mouse;

(ii) transforming the cell of (i) or a descendent of the cell by integrating into the cell's genome, a second DNA construct comprising DNA encoding a second indicator component not operably linked to a transcription control element;

(iii) producing tissue or specialized cells from the cell of (ii); and

(iv) selecting tissue or specialized cells of (iii) by the presence of a detectable indicator resulting from both the first and second indicator components.